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EXAMINER

EPPERSON, JON D

ART UNIT

PAPER NUMBER

1627

DATE MAILED: 09/09/2002 *ij*

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

File Copy

Application No.

09/742,033

Applicant(s)

SUN ET AL.

Examiner

Jon D Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 July 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 3,4 and 9-25 is/are pending in the application.
- 4a) Of the above claim(s) 23-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3,4 and 9-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 March 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **Detailed Action**

### ***Status of the Application***

1. Receipt is acknowledged of a response to an election of species requirement, which was dated on July 18, 2002 (Paper No. 10). Receipt of a Response and Amendment (Paper No. 8) and a Preliminary Amendment (Paper No. 6) is also acknowledged. The arguments presented in the Preliminary Amendment (Paper No. 6, pages 3-20) have not been considered as they pertain to a previous application that is not under examination (08/936,971 was abandoned on September 21, 2000) i.e., a response to a Final Action is NOT PROPER at this point in the litigation.

### ***Priority Claims***

2. This application claims priority under 35 U.S.C. 120 as follows:

CON of 08/936,971 (abandoned) WHICH is a  
CIP of 08/484,766 (abandoned) AND is a  
CIP of 08/880,209 (US Pat. No. 6,165,708) AND is a  
CIP of 08/880,210 (US Pat. No. 6,120,986) AND is a  
CIP of 08/880,353 (US Pat. No. 6,316,180)

Priority is granted in part for the reasons outlined below:

1) It is not clear what applications are claimed as priority documents. In the parent application (i.e., 08/936,971), applicants amended their priority claims as follows (see 09/936,971, Paper No. 8):

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“This application is a continuation-in-part of U.S. Serial No. 08/467,712 filed June 6, 1995; a continuation-in-part of U.S. Serial No. 08/928,0756 [08/928,075], filed September 11, 1997 etc.”

It would appear that this amendment should also apply to the present case since it is a continuation. However, applicants have not provided such an amendment. Correction is requested.

2) If applicant amends the specification to reflect the priority documents mentioned above in section 1, the priority claims can not be determined because the application 08/467,712 is awaiting decision by the board of appeals and is not available to the examiner.

3) Finally, support for the claims 9, 11, 14-17 has not been found in the priority documents cited. If applicant believes this is in error, the examiner asks the applicant to point to the support for the instant claims in each of the priority documents claimed.

Therefore, the effective filing date of the claims is the filing date of the parent case 08/936,971, which is **September 25, 1997**.

#### *Status of the Claims*

3. Applicant's response to the Restriction (Paper No. 8) and Election of Species (Paper No. 10) is acknowledged.

4. Claims 3-4 and 9-25 are pending in the present application because applicant canceled claims 1-2 and 5-8 without prejudice in paper No. 8. Consequently, applicants arguments/traversal to rejoin Groups I, III and IV (see Paper No. 8, pages 5-6) is moot because the claims have been cancelled by the applicant (see Paper No. 8, page 2) (“Please cancel claims 1, 2, 5, 6, 7 and 8 without prejudice”).

5. Furthermore, claims 23-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see below i.e., Response to Restriction and Election of Species with Traverse).

6. Therefore, claims 3-4 and 9-22 are examined on the merits in this action.

***Response to Restriction and Election of Species with Traverse***

7. Applicant’s election of Group II (claims 3-4) with traverse in Paper No. 8 is acknowledged.

8. The examiner finds applicant’s arguments to rejoin Group II with Group V persuasive (see Paper No. 8) and, as a result, the examiner will stipulate to rejoin Groups II (claims 3-4) and V (claims 9-12).

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9. The examiner does not find applicant's arguments to rejoin Groups I, III and IV convincing and, as a result, claim 23 (drawn to Group I), claim 24 (drawn to Group III) and claim 25 (drawn to Group IV) are withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim for the reasons outlined below. Claims 1-2 and 5-8 were cancelled without prejudice by applicant and are not considered.

10. The traversal to rejoin Groups I, III and IV is on the ground(s) that a "search of the compound would also encompass a search for methods using the same and kits or systems containing the same" and therefore does not represent a "significant burden" to the patent office. These arguments were fully considered but were not found persuasive. The traversal is addressed below.

As stated in the Restriction Requirement (Paper No. 7), these inventions have acquired a separate status in the art as shown by their different classification and/or divergent subject matter. The different methods and/or products would require completely different searches in both the patent and non-patent databases, and there is no expectation that the searches would be coextensive. Therefore, this does create an undue search burden for the Office.

11. Furthermore, the examiner does not find applicant's traversal of the species election (see Paper No. 10) convincing. Applicant claims that "a search of the prior art when examining the elected species will result in a search of the prior art when examining the non-elected species" and therefore does not represent a "significant

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burden” on the Patent Office. Applicants arguments were fully considered but not found persuasive.

As stated in the election of species requirement (see Paper No. 9), the examiner’s position is that the species are distinct, each from the other, because the structures and modes of action of each of the species encompassed are different. They would also differ in their reactivity and/or mechanism and/or the products made.

As also stated previously, the different species would require different searches and there is no expectation that the searches would be coextensive. The examiner maintains that this does create an undue search burden.

However, it was also stated that upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Finally, it was also stated that should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. This has not been done. Thus the species election is deemed proper and is maintained.

12. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

***Information Disclosure Statement***

13. The listing of references in the specification and the Information Disclosure Statement is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

14. The information disclosure statement filed April 23, 2001 (Paper No. 4) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The references that are listed in the Information Disclosure Statement have not been supplied with the case. The examiner requests that applicants send new copies of all references to be considered in the Information Disclosure Statement.

***Drawings***

15. Figure 1 is objected to for containing minor imperfections. Figure 1 lacks the single bond between the pyridine rings to complete the bipyridine ligand structures (compare Amino-tag to TPA-tag conjugates). These single bonds would NOT be deleted in this coupling reaction.



*Specification*

16. A new oath or declaration is required because a new oath or declaration cannot be amended and the original oath and declaration fail to claim priority to all of the applications set forth in the priority claim of the parent application from which this continuation depends.

*Claims Rejections - 35 U.S.C. 112, first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 3-4 and 9-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to compounds, which comprise "an electrochemiluminescent label linked to a coreactant, such that said compound emits electrochemiluminescence when exposed to electrochemical energy." In this case, applicants have not provided enough examples to demonstrate that they are

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in possession of the full scope of the invention as claimed. For example, it is not possible to know which ECL/CR pairs will have sufficient energy and react with sufficient speed (i.e., favorable reaction kinetics) *a priori* to produce the necessary electronically excited products. While, determining the free energy for a given set of Acceptor/Donor species may provide an answer for a limited number of ECL/RC pairs via a calculation of the standard electrochemical potentials i.e.,  $\Delta G^0 = E^0(A/A^-) - E^0(D^+/D)$  where A is an acceptor and D is a donor species (see specification, page 12), the specification does not provide teachings for more complicated reactions. For example, applicants claims would also encompass energy-deficient systems that generate light emission via triplet-triplet annihilation. Applicants have not provided any "formula" for calculating which ECL/RC pairs would fall under this category and since applicants do not "wish to be bound by a theoretical explanation of reaction mechanism" (see specification, page 11, lines 1-2), more complicated reactions of this type would be encompassed by the claims.

Furthermore, applicants have not provided sufficient guidance to determine what structural features of a given ECL/RC pair that would insure the favorable reaction kinetics that are required for these type of reactions or which ECL/RC pairs would demonstrate the required stability. Therefore, it is not clear which compounds fall within the scope of applicant's claims and, as a result, applicant cannot be in possession of the full scope of the invention.

Additionally, it is not possible to determine the limit of compounds that fall within the scope of these claims because the term "coreactant" encompasses "species which are capable of undergoing a chemical transformation to form said interactive

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species or said precursor species”, which would read on all compounds (given an infinite number of chemical transformations).

As a result, applicants have not demonstrated in “full, clear, concise, and exact terms” that they are in possession of the full scope of the claimed invention.

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention*. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). Therefore it is deemed that the disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus since the applicant has not disclosed **enough** specific examples of the elected invention. Moreover, the claimed genus encompasses members, which are yet to be prepared or envisioned.

2. Claims 3-4 and 9-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific coreactants disclosed, does not reasonably provide enablement for any coreactant. The specification does not enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use literally any coreactant. This is an enablement rejection.

The claims are directed toward a product which is a compound comprised of an ECL label linked to a coreactant. The disclosure teaches a number of specific coreactants including the beta-lactam moiety and ECL labels comprised of  $\text{Rb}(\text{by})_3$ . However, the preparation and use of coreactants which are present as precursors or species which can be transformed into a coreactant coupled to a generic ECL label does not appear to be within the scope of reasonable experimentation. The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands*, (U.S.P.Q. 2d 1400 (CAFC 1988)). The factors to be considered include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of the claims.

A number of factors would prevent one of skill in the art from practicing the invention without undue experimentation, these are summarized as follows:

1) The specification fails to give adequate direction and guidance as to all of the reactions which may be used to transform a compound into a reactive species or which precursors are useful. Moreover, the specification does not teach how to prepare such coreactant compounds, the specifics of the stability or the use. In addition the specification teaches limited ECL labels, specifically OS or  $\text{Rb}(\text{byp})_3$  and some Re pyridine complexes.

2) Applicants have provided limited working examples not commensurate in scope with the broad recitations of a "coreactant" or an "ECL label." There are also no

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examples of the complexes of ECL labels linked to coreactants commensurate in scope with the broad claims.

3) The breadth of the claims encompasses an indefinitely large number of compounds as it is unclear what is and is not transformable into an interacting species and hence what is a coreactant. The breadth of the claims also sets forth any ECL label to which any of the indefinitely large number of compounds will have to be linked to and remain functional.

4) The state of the prior art is such that a number of compounds that might be useful as coreactants have been prepared and even linked to ECL labels. Labels including the Re pyridine (see Massey cited below), Os and Rb(byp)<sub>3</sub> ECL labels have also been prepared and used.

5) The art is inherently unpredictable because it is not possible to know *a priori* which coreactant, especially those requiring transformation to form a potentially interacting species will be transformable when linked to an ECL label and actually function as predicted with an undefined series of undisclosed ECL labels. Moreover, it is not possible to know *a priori* which complexes will be capable of preparation, stable prior to use yet function under undisclosed assay conditions in the ECL assay. THE REASON that it is not possible to know these conditions a priori is because it is not possible to know which ECL/RC pairs will have sufficient energy and react with sufficient speed (i.e., favorable reaction kinetics) *a priori* to produce the necessary electronically excited products. While, determining the free energy for a given set of Acceptor/Donor species may provide an answer for a limited number of ECL/RC pairs via a calculation of the standard electrochemical potentials i.e.,  $\Delta G^0 = E^0(A/A^-)$ -

$E^0(D^+/D)$  where A is an acceptor and D is a donor species (see specification, page 12), the specification does not provide enablement for more complicated reactions. For example, applicants claims would also encompass energy-deficient systems that generate light emission via triplet-triplet annihilation. Applicants have not provided any "formula" for calculating which ECL/RC pairs would fall under this category and since applicants do not "wish to be bound by a theoretical explanation of reaction mechanism" (see specification, page 11, lines 1-2), more complicated reactions of this type would be encompassed by the claims. Furthermore, applicants have not provided sufficient guidance to determine what structural features of a given ECL/RC pair would insure the favorable reaction kinetics that are required for these type of reactions. Finally, as mentioned above, the stability of a given donor/acceptor is not predictable.

Therefore, while it is true that the level of skill in the art is high (references like Knight et al are not enough to enable the broad scope of the present claims), it would still require undue experimentation to make and use the coreactant-ECL label complexes commensurate in scope with the invention claimed in the absence of guidance from the applicant as set forth above.

***Claims Rejections - 35 U.S.C. 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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17. Claims 3-4 and 9-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 3-4 and 9-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3-4 and 9-22 recite a coreactant. However, the definition of a coreactant on page 6 includes both precursor species and species which are capable of undergoing transformation to form interactive species. In view of the foregoing, the claim is vague and indefinite because it is not possible to determine which components are, or are not, coreactants and what processes or transformations are being conducted. Hence, it would not be possible to know if one had infringed the instant claims when generating a compound which has an ECL label attached to any other molecule, as it would be unclear what process the attached molecule might be subject to that may transform it into a coreactant. Therefore, it is not possible to determine the metes and bounds of the invention as claimed.

B. Claims 3-4 and 9-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3-4 and 9-22 recite the term "linked" or depend on a claim that recites this term. This is vague and indefinite as it is unclear what the metes and bounds of "linked" are as utilized in the instant claims. For example does this mean covalently bound by a

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linker, or electrostatically attached or linked as in a redox couple without any bonds in between? Therefore, it is not possible to determine the metes and bounds of the invention as claimed. Providing a few examples of linkers in the specification is NOT ENOUGH for one of ordinary skill in the art to determine the metes and bounds of the invention as claimed.

C. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 21 recites the terms “strong oxidant” and “strong reductant”, which are relative terms that render the claim indefinite. The term “strong” is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

D. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 22 recites a coreactant that is a species capable of interacting with said electrochemical luminescent label to produce electrochemiluminescence or a precursor species which upon exposure to electrochemical energy is transformed into a species which is capable of interacting with said electrochemical label to produce electrochemiluminescence. This is vague and indefinite as it is not clear what compounds will meet these limitations. Therefore, it is not possible to determine the metes and bounds of the invention as claimed.



***Claims Rejections - 35 U.S.C. 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

(f) he did not himself invent the subject matter sought to be patented.

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

18. Claims 3-4, 10, 12-13 and 18-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Liang et al (Liang, P.; Dong, L.; Martin, M. T. "Light Emission from Ruthenium-Labeled Pencillins Signaling Their Hydrolysis by  $\beta$ -Lactamase" *J. Am. Chem. Soc.* **1996**, *118*, 9198-9199).

For *claim 3-4, 10, 12-13 and 18-22*, Liang et al discloses a  $\text{Ru}(\text{bpy})_3^{2+}$ -labeled 6-Aminopenicillanic Acid (Ru-APA) that is hydrolyzed by a  $\beta$ -lactamase (see Liang et al,

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page 9199, Figures 1 and 2), which reads on all the limitations in claims 3-4, 10, 12-13 and 18-22 because the Ru-APA contains a Ruthenium complex electrochemiluminescent label and a coreactant with a hydrolyzed  $\beta$ -lactam bond.

19. Claims 3, 11, 13, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) **1978**, *17*, 494-526).

For *claim 3, 11, 13, 14*, Faulkner discloses a compound which comprises an electrochemiluminescent label (anthracene acceptor) linked via a methylene chain to a coreactant (N,N-dimethylaniline donor) which emits electrochemiluminescence when exposed to electrochemical energy (see Faulkner, page 507, third paragraph with structure) ("Annihilation of the ions gives emission from the intramolecular exciplex"), which anticipates claims 3, 11, 13, 14 because the coreactant (N,N-dimethylaniline) is not an analyte of interest and the coreactant is a tertiary amine.

20. Claims 3-4, 10-14 and 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Massey et al WO 87/06706 (Date of Publication is **November 5, 1987**).

For *claim 3-4, 10-14 and 19-22*, Massey et al teaches a metal containing ECL label linked to a coreactant (see Massey et al, pages 144, 189 and 193 showing a Ru(bpy)<sub>3</sub> linked to another Ru(bpy)<sub>3</sub> and digoxigenin, Ru(bpy)<sub>3</sub> linked to a primary

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amine, and  $\text{Ru}(\text{bpy})_3$  linked to a theophylline, respectively), which reads on the limitations in claims 3-4, 10-14 and 19-22. The Digoxigenin conjugate on page 144 meets the limitation of claim 11 wherein "the coreactant is not an analyte of interest" because the coreactant is a  $\text{Ru}(\text{bpy})_3$  i.e., both the coreactant and the electrochemiluminescent label are  $\text{Ru}(\text{bpy})_3$  groups, which generate light via the following mechanism  $\text{Ru}(\text{bpy})_3^+ + \text{Ru}(\text{bpy})_3^{3+} \rightarrow \text{*Ru}(\text{bpy})_3^{2+} + \text{Ru}(\text{bpy})_3^{2+}$  (see Knight et al, page 884, equation 15) leaving the analyte of interest, digoxigenin or digoxigenin binding compounds, intact. Note:  $\text{*Ru}(\text{bpy})_3^{2+}$  emits light.

Theophylline and the primary amine shown on pages 189 and 193 would also be considered as coreactants within the definition provide by applicant because it is not clear what compounds fall within this definition (see 112 2<sup>nd</sup> paragraph rejection above for coreactant).

21. Claims 3-4, 10-12, 13-14 and 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Massey et al (US Pat No. 5,591,581) (Date of Patent is **January 7, 1997**; Date Filed is **April 15, 1994**).

Claims 3-4, 10-12, 13-14 and 19-22 are directed to a compound which is a ruthenium containing ECL labile linked via an amide bond to a coreactant which includes amines and tertiary amines wherein the coreactant can be a strong oxidant or a strong reductant.

For claims, 3-4, 10-12, 13-14 and 19-22, Massey et al discloses electrochemiluminescent labels with a coordinated Re atom linked to numerous

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compounds 'B' where B can be peptides, nucleic acids, polysaccharides, alkaloids, steroids, vitamins, amino acids or non-biological polymers (see Massey et al, claim 1). Massey also teaches amines linked to ECL labels (see Massey et al, column 15, lines 1-15; column 30, lines 38-column 31 line 37). Note that proteins have amine groups as well e.g., lysine side chains, etc. and well as alkaloids, polysaccharides that contain amino pentose and hexose units, and amino steroids, which reads on claims 3-4, 10-12, 13-14 and 19-22.

22. Claims 3-4, 10-12, 13-14 and 19-22 are rejected under 35 U.S.C. 102(f) and 102 (g) as being unpatentable over Massey et al (US Pat No. 5,591,581) (Date of Patent is **January 7, 1997**; Date Filed is **April 15, 1994**). The claimed subject matter appears to have been invented by Massey et al.

Claims 3-4, 10-12, 13-14 and 19-22 are directed to an invention not patentably distinct from claims 1-6 and 20 of commonly assigned 5,591,581. Specifically the applicant's are directed to the teachings of Massey et al '581 as applied under 35 USC 102(e) *supra*.

***Claim Rejections - 35 USC § 103***

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negated by the manner in which the invention was made.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

25. Claims 3-4, 9-17, 19, 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al (Knight, A. W.; Greenway, G. M. "Occurrence, Mechanisms and Analytical Applications of Electrogenenerated Chemiluminescence" *Analyst* **1994**, *119*, 879-890) in view of Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) **1978**, *17*, 494-526).

26. Knight et al teaches a large number of electrochemiluminescent compounds including  $\text{Ru}(\text{bpy})_3^{2+}$  complexes (see Knight et al, page 880, Table I, ruthenium complexes), which reads on claims 3-4, 9-19, 21-22. Knight also teaches a large number of coreactants including trialkylamines, NADH (see Knight et al, page 882, Table II,

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references 67, 79), which reads on claims 3-4, 9-17, 19, 21-22. Knight et al also teaches that ECL/coreactants can be used to detect biomolecules including amino acids, peptides and proteins (see Knight et al, page 884, column 2, line 12) and DNA (see Knight et al page 883, Table II, reference 82), which reads on claims 10 and 12.

The claimed invention differs from the prior art teaching of Knight et al by reciting the advantages to be gained by linking an EL with a CR. Knight et al does not teach the advantage of linking an EL with a CR. However, Faulkner does teach the advantages to be gained by linking an EL with a CR by describing the work of Itaya and Toshima which provides an example of an anthracene linked to an N,N-dimethylaniline.

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Knight et al with Faulkner as outlined above because both papers disclose compounds for electrogenerated chemiluminescence (i.e., each paper encompasses overlapping subject matter e.g., both papers show the use of anthracene and tertiary aromatic amines in electrogenerated chemiluminescence).

Furthermore, one of ordinary skill in the art would have been motivated to use the EL and CR compounds as taught by Knight with a linker to join the EL with the CR as taught by Faulkner because Faulkner specifically states the “advantages” of linking an EL to a CR (see Faulkner, pages 507-508) (“The linked systems [provide] an unusually efficient exciplex emission ... Note also that [the linked exciplex] is stabilized in a polar medium, rather than being destabilized as true exciplexes are. It is not surprising [i.e., it’s obvious] that its chemiluminescence is very much brighter than that from the usual

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exciplex systems in polar solvents). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Faulkner et al shows a working example of applicant's invention e.g., the anthracene linked to the N,N-dimethylaniline via a methylene chain (see Faulkner, page 507, third paragraph).

### ***Double Patenting***

27. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

28. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

29. Claims 3-4 and 9-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 19-20 of U.S. Patent No. 5,591,581. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 3 and 4 are directed to a compound which is a metal containing ECL labile linked to a coreactant because Massey et al discloses electrochemiluminescent labels with a coordinated Re atom linked to numerous compounds (B) where B can be peptides, nucleic acids, polysaccharides, alkaloids, steroids, vitamins, amino acids or non-biological polymers (see claim 1 for example). As a coreactant includes precursor species and species which upon the chemical transformation which result in species which can interact with the label to induce electrochemiluminescence Massey et al anticipates claims 3-4.

In addition, U.S. Patent No. 5,591,581 also amines linked to ECL labels.

30. Claims 3-4 and 9-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,643,713. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Compounds which comprise an electrochemiluminescent label linked to a coreactant as set forth in claims 3 and 4 of the instant application are substantially identical if not identical to those set forth in US



5,643,713, claims 1 and 6, although recited in slightly different language or by structure. One of ordinary skill in the art would recognize that the coreactant as recited in claims of the instant application are equivalent to the chemically transformable first compound as set forth in claim 1 of the 5,643,713 patent and have the properties recited in section I of the claim and undergo the reaction as set forth in section II of the claim.

Furthermore, there is no apparent reason why applicants were prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

In addition to the teachings previously recited note that claim 6 recites an aromatic coreactant.

#### ***Status of Claims/Conclusion***

31. No claims are allowed.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 pm.

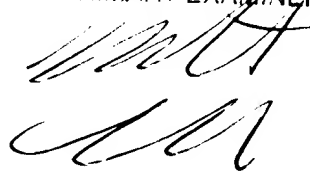
33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (703) 308-4537. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

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34. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.  
September 3, 2002

BENNETT CELSA  
PRIMARY EXAMINER

Handwritten signature of Bennett Celsa, consisting of stylized cursive letters.